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October 25, 1999

BY HAND DELIVERY

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

RE: Docket No. 99D-2096: Draft Guidance Interpreting Sameness of Monoclonal Antibody Products Under the Orphan Drug Regulations (July 26, 1999)

Dear Sir or Madam:

I appreciate this opportunity to comment on FDA's draft guidance regarding monoclonal antibodies (MABs) and orphan drug exclusivity. Beginning in January 1984 while I was with the Agency, I was asked to assist in developing the policies and procedures for implementing the Orphan Drug Act, which had just become law in 1983. From that time until now I have had a healthy respect for the public health benefits that have been achievable through the orphan drug law.

The law's chief incentive or spur to orphan drug research and development has been, and remains, orphan drug exclusivity. I understand the Agency's difficulty in balancing the incentives of the Orphan Drug Act with the need to encourage research and development of "different" therapeutic agents. However, in my opinion, FDA's focus on the amino acid sequence within the CDRs as the principal criterion for determining whether one MAB is structurally the same as another MAB has the potential for eviscerating the Orphan Drug Act of its most potent spur to orphan drug research and development. For example, I understand that two MABs may have very different amino acid sequences, yet both can bind to the same receptor and provide the same therapeutic benefit. Under the draft guidance document, subsequent MABs would almost always be

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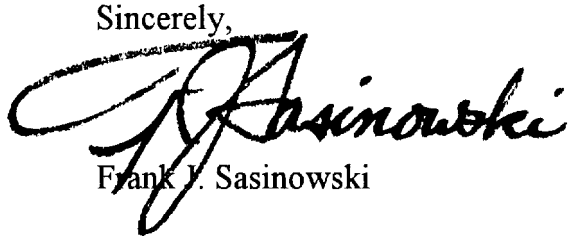
structurally distinct, with the result that the pioneer's orphan drug marketing exclusivity for a MAB would be rendered essentially worthless.

I am also troubled more generally by FDA's apparent devaluation of market exclusivity in the draft guidance. For the last decade, orphan drug exclusivity has proven to be the essential stimulus for the development of numerous novel therapeutic agents. To devalue that stimulus now, when so many novel therapeutic modalities (e.g., gene therapy) are on the horizon, sends the wrong message to both the biotechnology industry and to patients with rare disorders. If FDA devalues orphan drug exclusivity for MABs, neither industry nor patients can be sure what the Agency will do the next time a novel orphan drug exclusivity issue arises. By attempting to navigate this slippery slope using the approach in the draft guidance, FDA leaves all of its stakeholders confused, wary, and cautious given the position expressed in the draft guidance that is incompatible with exclusivity.

In 1990, FDA was faced with the difficult task of proposing a definition of orphan drug "sameness" for macromolecules in general. I observed first-hand how the expert panel of scientists from the Institute of Medicine contributed immeasurably to the process.' They carefully considered several alternatives and presented their collective reasoning and conclusions to the Agency. The efforts of that process contributed greatly to FDA's assessment of the policy implications of each alternative approach that the Agency was considering at that time. The resulting regulation promulgated by FDA has over the years served well the Agency, industry and patients with rare disorders. Given the success of that previous process, FDA would do well to convene a similar panel of experts, including all stakeholders, to assist the Agency in determining how "sameness" should be defined with respect to MABs in the context of the Orphan Drug Act.

Sincerely,



Frank J. Sasinowski

FJS/dng

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[1] Report of a Workshop, "Microheterogeneity of Biological Macromolecules," Forum on Drug Development, 199 1, Division of Health Science Policy, Institute of Medicine (see 57 Fed. Reg. 62076, 62080 (Dec. 29, 1992)).